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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,323	09/26/2005	Frank Striggow	LNK-007	8223

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SMITH PATENT CONSULTING CONSULTING, LLC
3309 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
CLARK, AMY LYNN	

ART UNIT	PAPER NUMBER
1655	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,323	STRIGGOW ET AL.	
	Examiner	Art Unit	
	Amy L. Clark	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 15-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 15-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment is made of the receipt and entry of the amendment filed on 11/03/2008 with the amendment of claims 1, 7, 8, 10, 11, and 15, and the cancellation of claims 12-14.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-11 and 15-19 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating Alzheimer's disease comprising administering to a patient in need of such a treatment, an effective dosage of the medicament comprising at least one of the following: incense (olibanum), incense extract, biologically active substances contained in incense and boswellic acid, wherein the extracts are obtained by extraction with chloroform: methanol, does not reasonably provide enablement for a method for treating cerebral ischemia comprising the step of administering to a subject in need thereof a medicament comprising a neuroprotective amount of an active ingredient comprising a hydrogenation production of *Boswellia serrata* obtained through the catalytic hydrogenation of ethanol extracts of frankincense (*Boswellia serrata*). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

This rejection is maintained for reasons of record set forth in the previous office action and for the reasons provided below.

Enablement is considered in view of the *Wands* factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: Claim 1 is drawn to a method for treating cerebral ischemia comprising the step of administering to a subject in need thereof a medicament comprising a neuroprotective amount of an active ingredient comprising a hydrogenation production of *Boswellia serrata* obtained through the catalytic hydrogenation of ethanol extracts of frankincense (*Boswellia serrata*). Claim 2 further claims that the cerebral ischemia of claim 1 occurs as a result of apoplexy.

The nature of the invention is complex in that claim 1 is drawn to a method for treating cerebral ischemia comprising the step of administering to a subject in need thereof a medicament comprising a neuroprotective amount of an active ingredient comprising a hydrogenation production of *Boswellia serrata* obtained through the catalytic hydrogenation of ethanol extracts of frankincense (*Boswellia serrata*). However, the way the claim is presently written, cerebral ischemia could result from any source and that regardless of the source, it can be treated. It should be noted that cerebral ischemia is an ischemic condition where the brain or parts of the brain do not

receive enough blood flow to maintain normal neurological function and that cerebral ischemia can be the result of various diseases or the result of arterial obstruction, such as strangulation.

Breadth of the Claims: The claims are broad in that cerebral ischemia is treated in a subject comprising the step of administering to a subject in need thereof a medicament comprising a neuroprotective amount of an active ingredient comprising a hydrogenation production of *Boswellia serrata* obtained through the catalytic hydrogenation of ethanol extracts of frankincense (*Boswellia serrata*). The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims.

Guidance of the Specification and Existence of Working Examples: The specification discloses a method of observing the effect of a frankincense extract containing boswellic acid on the infarct volume after experimentally induced transient focal cerebral ischemia (apoplexy), wherein Applicant discloses a method of experimental induction of a focal ischemia by intracerebral microinjection of endothelin 1 in the vicinity of the middle cerebral artery (eMCAO) and using Sprague Dawley rats, wherein the rats are intraperioneally injected with frankincense extract (See pages 16-19 of the originally filed specification). Please note that it appears that Applicant is disclosing a frankincense extract containing boswellic acid as the extract used in these trials. However, it should be noted that no other information is provided disclosing what the extract actually is or how it is obtained in the working examples, therefore, it is unclear for what Applicant is actually enabled.

Please note that while it is possible that damage from cerebral ischemia may be decreased, prevention of cerebral ischemia would require that a person is not exposed to any factors that could cause cerebral ischemia, such as strangulation. Therefore, Applicant is not enabled for prevention and/or treatment of cerebral ischemia.

Predictability and State of the Art: The state of the art at the time the invention was made was unpredictable and underdeveloped. For example, Singer et al. (U*, 'Associated systemic factors in cerebrovascular ischemia', South Med J. Vol. 69, No. 6 (June 1976) pp. 709-714) teaches that systematic disorders, such as cardiac disorders, are commonly recognized as predisposing and sometimes actual precipitating events in cerebral ischemia. Singer further teaches that a one-year comprehensive investigation of all patients with ischemic brain disease revealed that brain ischemia is more commonly precipitated by system illness than usually supposed, particularly transient ischemic attacks of the vertebrobasilar circulation and completed infarcts in the carotid distribution and that cardiac disorders outnumber all other precipitating events.

Braune et al. (V*, 'Cerebral infarct in the circulatory area of the arterial cerebrial media following chiropractic therapy of the cervical spine', Dtsch Med Wochenschr, Vol. 116, No. 27 (July 1991) pp. 1047-1050) teaches that chiropractic manipulation of the neck can occasionally cause severe neurological complications.

Based upon the fact that the actual underlying cause of cerebral ischemia is unknown, it is doubtful that Applicant's claimed invention can prevent cerebral ischemia, and that Applicant's invention can treat all types of cerebral ischemia, wherein cerebral ischemia or treat cerebral ischemia that occurs as a result of apoplexy.

Chen et al. (W*, "Combination therapy for ischemic stroke: potential of neuroprotectants plus thrombolytics". Am. J. Cardiovasc. Drugs, Vol. 2, No. 5 (2002) 303-313, Abstract only) teaches that cerebral ischemia triggers a number of pathophysiological and biochemical changes in the brain that present potential targets for therapeutic intervention. Although several neuroprotective agents which block cell death pathways have been proposed to have therapeutic potential in patients with stroke (apoplexy) results from clinical trials have been disappointing. Finally, PCMR Research: Animal Experimentation Issues (X*) teaches that stroke is the third leading cause of death in the U.S., but strokes and the conditions that lead to them are rare in rats and other animals. PCMR Research: Animal Experimentation Issues further teaches that animal "models" of stroke have been developed, but their usefulness has been severely criticized by the scientific community and that according to researchers at the University of Iowa and the Mayo Clinic in Rochester, Minnesota, although animal models of cerebral ischemia have been used extensively to test new therapies in human stroke, their record for identifying clinically effective drugs has been disappointing. PCMR Research: Animal Experimentation Issues further teaches of 25 compounds which were helpful in laboratory animal models of stroke, none worked on people and that an over-reliance upon such models may impede rather than advance scientific progress in the treatment of this disease. Therefore, irrespective of Applicant's working examples involving rats, it has not been established that rats are an adequate model for stroke in humans and there is no evidence that Applicant's claimed invention will have the desired effect in humans.

Thus, while the claim-designated method may be useful for providing such an effect, Applicant does not disclose a method of treating cerebral ischemia comprising the step of administering to a subject in need thereof a medicament comprising as an active ingredient a hydrogenation product of *Boswellia serrata* obtained through the catalytic hydrogenation of ethanol extracts of frankincense (*Boswellia serrata*).

Amount of Experimentation Necessary: The quantity of experimentation necessary to carry out the claimed invention is high, as the skilled artisan could not rely on the prior art or instant specification to teach how to make and use a medicament comprising hydrogenation products of frankincense extracts for treating cerebral ischemia or treating cerebral ischemia, wherein the cerebral ischemia occurs as a result of cardiac infarction in humans. In order to carry out the claimed invention, one of ordinary skill in the art would have to identify a medicament comprising hydrogenation products of frankincense extracts that can be administered in a therapeutically effective dose with an acceptable level of side-effects. Please note that the way the claims are currently written, that Applicant does not state that a therapeutically effective amount of a hydrogenation product of *Boswellia serrata* obtained through catalytic hydrogenation of ethanol extracts of frankincense (*Boswellia serrata*).

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an undue amount of experimentation to make and/or use the claimed invention. Therefore, claims 1-11 and 15-19 are not considered to be fully enabled by the instant specification.

Applicant's arguments have been thoroughly considered, but the rejection remains the same for the reasons set forth in the previous Office action and for the reasons set forth below.

Applicant argues that the test of enablement is whether one reasonably skilled in the art could make or use the claimed invention from the disclosures in the specification, coupled with information known in the art without undue experimentation. Applicant further argues that it is not necessary to describe each and every parameter, such as dosage, route and method of administration with specificity. Applicant further argues that prior art teaches using the *Boswellia* extracts Sallaki ® and H15 ® for the treatment of inflammatory diseases, thereby establishing that medicinal formulations of frankencense extracts were known in the art at the time the invention was made. Applicant further argues that hydrogenation products of *Boswellia* extracts were also known.

In response to Applicant's arguments, first of all, Sallaki ® and H15 ® are trademarks/trade names and cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. Further, Applicant is claiming hydrogenation products of *Boswellia* extracts obtained through catalytic hydrogenation of ethanol extracts. Applicant does not demonstrate a method of making these claimed extracts nor does Applicant demonstrate that these particular extracts are even tested and provide the claim-designated results of being able to treat cerebral ischemia.

Applicant is further directed to MPEP 2164.03, wherein the MPEP states:

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. **In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling.** See, e.g., *Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004),

The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. On the other hand, **if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art**. Accordingly, what is known in the art provides evidence as to the question of predictability. *In re Marzocchi*, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971). *In re Vickers*, 141 F.2d 522, 526-27, 61 USPQ 122, 127 (CCPA 1944); *In re Cook*, 439 F.2d 730, 734, 169 USPQ 298, 301 (CCPA 1971); *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938); *In re Fisher*, 427 F.2d 833,

839, 166 USPQ 18, 24 (CCPA 1970) . See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991).

Applicant further argues that Applicant is not required to show that a therapeutic treatment is completely safe or to prove clinical efficacy to show that a therapeutic process is operable.

In response to this argument, Applicant is confusing enablement with utility. These are two separate issues. This rejection is drawn to enablement, not utility. With regards to showing amounts of treatment to administer, since the art does not recognize that extracts of this nature are useful for treating cerebral ischemia, as claimed by Applicant, the amounts of the ingredient administered cannot be determined and it is unclear as to what a safe range of dosage may be administered or what amount may be administered to have the claimed functional effect.

Applicant further argues that the reference written by PCRM is biased because PCRM is an animal activist group.

In response to Applicant's argument regarding the references, please note that Applicant's submitted reference "Rodent Models of Focal Stroke: Size, Mechanism and Purpose" by S. Thomas Carmichael teaches that the mechanism, and purpose, selected rodent models can be used to study the major targets of human neuroprotective therapies--reperfusion injury, delayed apoptotic cell death, and inflammatory cascades. However, rodent models have many well-recognized limits, such as differences in tolerance to cerebral edema and important molecular differences

in thrombotic, inflammatory, and DNA repair cascades compared with primates. In reality, biomedical funding and space constraints make the animal modeling of stroke a progressive endeavor (See page 405). Carmichael further teaches that less than 10 rodent models of focal stroke are routinely used in experimental study and that they vary widely in their ability to model human disease and in their application to the study of cell death or neural repair. Therefore, Carmichael teaches that the type of model used varies in its ability to model human disease. Furthermore, Carmichael is discussing rat models and their testing in primates, not their correlation to testing in humans. Therefore, based on the fact that the rodent model used can provide variable results and that the models have limitations, Carmichael further illustrates the fact that the art does not recognize a successful correlation between testing in rats and humans with regards to treating ischemia, the model provided by Applicant in the specification does not demonstrate efficacy in humans.

Please note the following art rejections are made based upon what was known in the art at the time the invention was made. If not all claims are rejected under art, this does not mean that these claims are allowable, since all of the claims examined are rejected under 112 1st paragraph as lacking full enablement, as discussed above.

Claim Rejections - 35 USC § 102

Claims 1, 3, 4, 7-9 and 16-19 remain rejected under 35 U.S.C. 102(b) as being anticipated by Etzel (A*, US 5,720,975).

Etzel teaches a method of treating Alzheimer's disease comprising administering to a patient in need of such a treatment, an effective dosage of the medicament comprising at least one of the following: incense (olibanum), incense extract, biologically active substances contained in incense and boswellic acid (See abstract and claim 1). Etzel further teaches that the medicament can be administered orally, intraperitoneally, buccally, rectally, intramuscularly or topically and that the form of the medicament is a tablet, capsule, injectable solution, solution, salve, emulsion or creme (See claims 7 and 8). Etzel further teaches that *Boswellia serrata*, which reads on a boswellic-acid containing vegetable preparation and a frankinsense of boswellic acid-containing vegetable extract, is the preferred incense plant that contains boswellic acid and that the extracts are obtained by extraction with (4.2-5.9:1) chloroform: methanol (See column 2, lines 34-46), which reads on the limitations of claims 3, 4, 7-9, 11 and 16-19.

Therefore, the reference anticipates the claimed subject matter.

Applicant argues that Etzel does not teach the claimed invention of claim 1 because Etzel teaches a method of treating Alzheimer's disease with an extract of frankinsense, which is different than a hydrogenation product of frankinsense.

In response to Applicant's argument, the rejection is maintained because this is what Applicant is enabled for, as clearly set forth above.

Claim Rejections - 35 USC § 103

Claims 1, 3-11 and 15-19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Etzel (A*, US 5,720,975), in view of Badria et al. (U1*).

The teachings of Etzel are set forth above and applied before. Etzel further teaches that incense resins may be used as a source of extracts, that the incense resin can be obtained from a *Boswellia* plant, wherein the *Boswellia* plant can be *Boswellia serrata* and that *Boswellia carterii*- misspelled by Etzel as *Boswellia carteri*- is also an example of an incense plant useful in Etzel's invention). Please note that *Boswellia carterii* resin intrinsically contains 3-oxo-tirucallic acid, 3-hydroxy-tirucallic acid, β-boswellic acid and 11-keto-boswellic acid (See Badria et al.).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the source of boswellic acid taught by Etzel because at the time the invention was made, it was known that Alzheimer's disease could be treated by administering to a patient in need of such a treatment, an effective dosage of a medicament comprising at least one of the following: incense (olibanum), incense extract, biologically active substances contained in incense and boswellic acid, as clearly taught by Etzel, as was that incense resins may be used as a source of extracts and that *Boswellia carterii* is also a useful source of incense (olibanum), incense extract, biologically active substances contained in incense and boswellic acid, as clearly taught by Etzel.

Finally, one of ordinary skill in the art would have been motivated and one would have had a reasonable expectation of success to use incense (olibanum), incense extract, biologically active substances contained in incense and boswellic acid obtained from *Boswellia carterii* or a resin of a *Boswellia* plant, wherein the *Boswellia* plant can

be *Boswellia serrata* in a medicament for treating Alzheimer's disease, as clearly taught by Etzel.

Based upon the beneficial teachings of the cited references, the skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Applicant argues the same point as above under 102(b) and the Examiner's response is the same.

Applicant argues that the Badria reference was published after the filing of Applicant's invention. In response to this argument, the Badria reference was used merely to illustrate that *Boswellia* extract intrinsically contains the compounds claimed by Applicant, snce *Boswellia* extract always contained these compounds.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy L. Clark whose telephone number is (571) 272-1310. The examiner can normally be reached on Monday to Friday between 8:30am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christopher R. Tate/
Primary Examiner, Art Unit 1655

Amy L. Clark, AU 1655
January 12, 2009